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Nonlinear Analysis of Postural Sway in Multiple Sclerosis

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***Abstract*—**Multiple Sclerosis (MS) is a disease which affects the central nervous system and causes balance problem. In clinical, this disorder is usually evaluated using static posturography. Some linear or nonlinear measures, extracted from the posturographic data (i.e. center of pressure, COP) recorded during a balance test, has been used to analyze postural control of MS patients. In this study, the trend (TREND) and the sample entropy (SampEn), two nonlinear parameters were chosen to investigate their relationships with the expanded disability status scale (EDSS) score. 40 volunteers with different EDSS scores participated in our experiments with eyes open (EO) and closed (EC). TREND and 2 types of SampEn (SampEn1 and SampEn2) were calculated for each combined COP's position signal. The results have shown that TREND had a weak negative correlation to EDSS while SampEn2 had a strong positive correlation to EDSS. Compared to TREND and SampEn1, SampEn2 showed a better significant correlation to EDSS and an ability to discriminate the MS patients in the EC case. In addition, the outcome of the study suggests that the multi-dimensional nonlinear analysis could provide some information about the impact of disability progression in MS on dynamics of the COP data.

***Keywords*—**Balance, multiple sclerosis, nonlinear analysis, postural sway.

I. Introduction

MULTIPLE SCLEROSIS (MS), one of the common autoimmune diseases of the central nervous system, can cause damage to parts of the nervous system and lead to balance, movement and vision disorders. The expanded disability status scale (EDSS), a clinical tool developed by J. F. Kurtzke [1], is widely used for quantifying disability of people with MS. It is an ordinal rating scale ranging from 0 (normal neurological examination) to 10 (death due to MS) in 0.5 unit increments. Scoring is based on measures of impairment in 8 functional systems: brain stem, pyramidal, cerebral, cerebellar, bowel, and bladder, sensory, visual, and other. If a MS patient is still able to walk without aid, his EDSS score will be less than 5.0. Once he loses the ambulatory ability, his EDSS score will be equal to or more than 5.0.

Balance problems are common in people with MS and their causes are not well understood. Static posturography, a commonly used non-invasive technique to quantify balance in MS, is carried out by asking the patient to stand quietly on a force platform, which is able to detect the oscillations of the body. With the help of this technique, we can obtain the time-dependent trajectory of the center of pressure (COP) of the patient and extract many linear and non-linear parameters to assess postural control of the patient. Several studies in MS [2], [3] have shown that COP sway is significantly higher in MS patients than in controls. Our previous studies [4], [5] have demonstrated that there is a significant correlation between the EDSS and some measures of recurrence quantification analysis (RQA) extracted from the COP data, such as recurrence rate (RR).

Although changes of postural control strategy in MS have been reported [6], [7], few studies have focused on the correlation between these changes and the EDSS and discussed whether they are able to discriminate patients of different EDSS scores. Thus, two parameters referring to the strategy were chosen to perform such an investigation: the trend (TREND) and the sample entropy (SampEn). The purpose of this paper was to verify whether both parameters could be used to classify MS patients by assessing their relationships with the EDSS score in both eyes open and closed cases.

II. Materials and Methods

A. Experiments

30 patients (6 males and 24 females, age 47.43 ± 10.28) and 10 healthy subjects (2 males and 8 females, age 43.67 ± 7.45) participated in our study which took place in the Saint-Philibert Hospital (Lomme). The clinical EDSS scores established by a well-trained neurologist were 0, 1.5, 2.5 and 3.5, i.e. 10 participants per category. No one had orthopedic problems. The balance measurement was performed using a Satel force platform with a sampling frequency of 40 Hz. During the recording, the subject stood upright on the platform with bare feet and arms by his/her side. Each participant performed two trials, one with eyes open (EO) and the other with eye closed (EC), with a rest period between them to avoid the effects of fatigue. Each trial lasted 51.2 seconds. COP's sway data in both medial-lateral (X) and anterior-posterior (Y) directions of the subject were then collected so as to be analyzed using Matlab.

B. Calculated Parameters

Two nonlinear parameters, the trend (TREND) and the sample entropy (SampEn), were involved in this study.

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1. TREND

TREND, providing information about the stationarity of the dynamic system, is a measure of RQA in which the state space of a dynamic system is reconstructed from a single scalar time series through embedding [8]. Before calculating this nonlinear measure, three embedding parameters must be determined, i.e. time delay (τ) and embedding dimension (m), as well as the threshold (radius) to identify recurrent points [9].

TREND represents a linear regression coefficient of the relationship between the recurrence point density in a diagonal line parallel to the main diagonal and the distance from this line to the main diagonal [8]:

$$TREND = \frac{\sum_{k=1}^{N}(k-\tilde{N}/2)(RR_k - \langle RR_k \rangle)}{\sum_{k=1}^{N}(k-\tilde{N}/2)^2} \quad (1)$$

where $\tilde{N}$ is the maximal number of diagonals parallel to the main diagonal, <·> represents the average value and RR_k

$$RR_k = \frac{1}{N-k}\sum_{j-i=k}^{N-k} R(i,j) \quad (2)$$

is the percentage of recurrence in a diagonal line parallel to the main diagonal of distance k. $R(i,j)$, either 0 or 1, refers to the value of the point at (i,j) in the recurrence plot (RP). In other words, TREND is the slope of line-of-best-fit through RR as a function of the displacement from the main diagonal. In practice, as recurrence point densities are very low in the edges of the RP, the last 10% range is often excluded in order to avoid the edge effects.

2. SampEn

SampEn is a measure basically quantifying the irregularity of a time series. For a given embedding dimension (m), tolerance (r) and number of data points (N), we take the negative logarithm of the probability that if the distance between two template vectors of length m is less than r then the distance between two template vectors of length $m+1$ is also less than r.

$$SampEn(m,r,N) = -\log(A(r)/B(r)) \quad (3)$$

where $A(r)$ (or $B(r)$) is the total number of template matches in a ($m+1$)-dimensional (or m-dimensional) phase space within a distance tolerance r [10].

C. Data Analysis

In order to analyze overall postural sway of the subject during recording, a combined COP's position signal (P) was first calculated for each trial as:

$$P(i) = \sqrt{(P_x(i))^2 + (P_y(i))^2} \quad (4)$$

where $P_x(i) = X(i+1) - X(i)$, $P_y(i) = Y(i+1) - Y(i)$. $X(i)$ and $Y(i)$ represent COP's X and Y coordinates at the instant i, respectively. TREND and SampEn were then computed for each COP's position signal.

To calculate TREND, the COP time series was first reconstructed into a multidimensional state space using $m = 3$, $\tau = 15$ sample and the RP was then obtained using radius = 20% * MD (mean distance between the vectors in the reconstructed space) [11]. Finally, TREND was computed using (1). For SampEn, the length of the template pattern was defined as $m = 3$. As there are 2 ways to define the tolerance (r) in the previous studies, 2 types of SampEn were investigated in this study: SampEn1 was calculated using $r = 0.2$ * SD (standard deviation of the time series) [12], and SampEn2 was calculated using $r = 0.2$ [10].

The Spearman's correlation coefficient (R) was finally computed between each calculated parameter and the EDSS. The difference between the experimental conditions (EO vs EC) was analyzed by Sign test, whereas the difference between the EDSS scores was analyzed by Mann-Whitney U-test (if there are only two groups) or by Kruskal-Wallis test (if there are more than two groups).

III. Results

Correlation coefficients (R) between the calculated parameters and the EDSS score are shown in Table I. The correlation between TREND and EDSS was neither significant in EO case nor in EC case. Although all correlations between SampEn and EDSS were significant, compared to SampEn1, SampEn2 was more correlated to EDSS in both EO and EC cases.

TABLE I
Correlation Coefficients (R) between the Calculated Parameters (TREND and SampEn) and the EDSS Score in the Eyes Open (EO) and Closed (EC) Cases

Correlation coefficients (*R*)	**EO**	**EC**
TREND vs EDSS	- 0.13	- 0.15
SampEn1 vs EDSS	0.52**	0.33*
SampEn2 vs EDSS	0.64***	0.76***

*: p<0.05; **: p<0.001; ***: p<0.0001.

Although the absolute TREND was significant greater ($p<0.05$) in the EO than in the EC for EDSS = 2.5 and EDSS = 3.5 (Fig. 1), there was no significant change ($p>0.05$) from EDSS = 1.5 to EDSS = 3.5, nor between the healthy subjects and the MS patients on both EO and EC conditions.

For the SampEn1 of the COP's position, there was a significant increase ($p<0.001$) between the healthy subjects and the MS patients in both EO and EC cases (Fig. 2). However, the difference among the patients was not significant. Moreover, there was no significant change between EO and EC for almost EDSS scores except EDSS = 3.5 ($p<0.005$). In contrast, SampEn2 increased significantly from EDSS = 1.5 to EDSS = 3.5 in the EC ($p<0.005$) (Fig. 3). In addition, there was a significant difference between the healthy subjects and all MS patients ($p<0.0001$) in both cases, as well as between EO and EC ($p<0.005$) for almost EDSS scores except EDSS = 1.5.

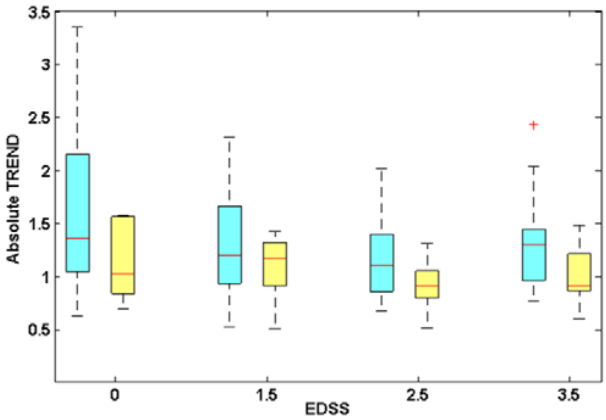

Fig. 1 Relationship between the absolute TREND for the COP's position and the EDSS score in the eyes open (blue) and closed (yellow) cases

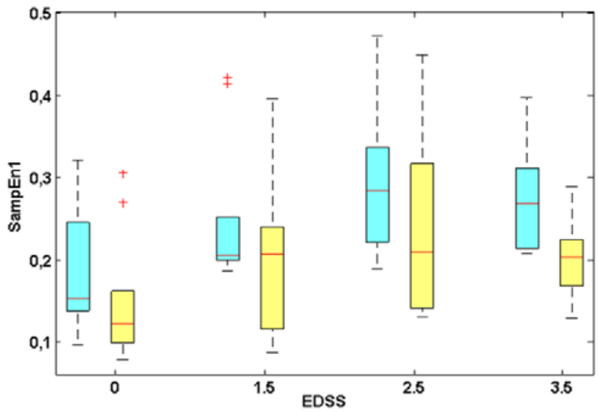

Fig. 2 Relationship between SampEn1 for the COP's position and the EDSS score in the eyes open (blue) and closed (yellow) cases

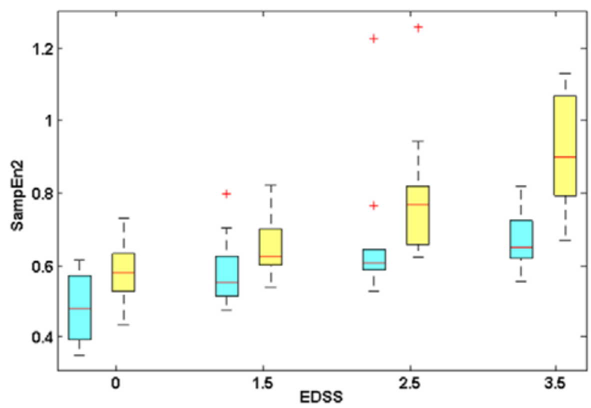

Fig. 3 Relationship between SampEn2 for the COP's position and the EDSS score in the eyes open (blue) and closed (yellow) cases

IV. Discussion

Human postural performance can be quantified by linear or nonlinear measures of COP data collected during quiet standing [13]. As impairment of postural control is an important symptom of MS, several studies have used linear or nonlinear analyses for evaluating the postural control of MS patients or exploring the dynamical structure of postural sway in MS patients [6], [7]. Among all measures of COP signal, TREND and SampEn are two important nonlinear measures, which reflect temporal structure of sway variability. Although these two measures were used for examining dynamics of the time series of the COP in some diseases [13], [14], only the difference between healthy controls and patients has been reported and few investigations have been performed between patients with different degrees of a disease. On the basis of the fact that we had observed a significant correlation between the EDSS and some measures of the COP data in [5], the purpose of this study was to verify whether, TREND and SampEn, these two non-linear measures possess this property and can be further used to classify MS patients in both EO and EC cases. For this, we calculated the Spearman's correlation coefficient (R) between the EDSS and each nonlinear parameter computed with m = 3. TREND had a weak negative correlation to EDSS (R = -0.13 in EO, R = -0.15 in EC) while SampEn2 had a strong positive correlation to EDSS (R = 0.64 in EO, R = 0.76 in EC). Compared to SampEn1, SampEn2 showed a better significant correlation to EDSS and an ability to discriminate the MS patients in both experimental cases.

TREND is a RQA measure quantifying the level of the stationarity of the time series system. The lower the absolute TREND is, the more stationary the system is [8]. As the COP data are generally recorded in both X and Y directions, it is possible to obtain different results for these two directions. In a previous study in MS [7], a significantly lower TREND was observed in the EC than in the EO ($p<0.04$) in X direction while no significant difference was observed in Y direction. In order to evaluate postural sway of the whole body, we combined the recorded COP data, as mentioned in the Section II. C, and then calculated the TREND of the combined X–Y data. In our study, three conclusions could be drawn from the TREND of the combined X–Y COP data: (1) there was no significant difference ($p>0.05$) between the healthy subjects and the patients in both EO and EC; (2) there was no significant difference ($p>0.05$) between EO and EC for EDSS = 0 and EDSS = 1.5; (3) it was significantly smaller ($p<0.05$) in EC than in EO for EDSS = 2.5 and EDSS = 3.5. The significant decrease in TREND of the COP's position signal for the MS patients in the EC case may be a behavioral reflection of their abnormal postural control. Postural sway during the balance test results from the interaction between internal factors affecting and helping maintain the balance of the body [8]. Thus, balance impairments caused by MS will be reflected in altered characteristics of postural sway.

SampEn is a nonlinear measure to quantify the irregularity of a time series. An increase in SampEn indicates in itself a higher level of disorder and unpredictability in a time series. On the basis of the selection of the tolerance *r*, 2 types of

SampEn were involved in this study: SampEn1 and SampEn2. Despite this, for both SampEn1 and SampEn2 of the COP's position, there was a significant increase between the healthy subjects and the MS patients in EO and EC. This consistent result has shown that COP data of the patients are more unpredictable than the ones of the healthy participants.

Our results showed a significantly higher SampEn2 in EC than in EO for almost EDSS scores. This is in agreement with some studies [10], and different from some ones [15]. These contradictory results could be related to the analyzed data. Note that the analyzed data in all these studies were the COP increment signals (i.e. the velocities) not the COP time series. Increase of SampEn2 in the EC condition may be due to the lack of visual input. When there is no visual feedback during a quiet standing, the subject cannot effectively regulate his body to maintain balance. This fact could result in the increase of the irregularity of the combined COP signal (i.e. increase of SampEn2). The results indicated also a significantly increase in SampEn2 with the increase of EDSS. As we know, COP's sway (postural disorders) is significantly smaller in controls than in the MS group [2], [3]. This could be considered as an increase of internal noise related to the neurological disorders. As these disorders (i.e. noise) could influence the precision of postural regulation, the subject may spend a longer time on achieving balance. This fact may affect temporal structure of postural sway variability and result in a more irregular COP's position signal. Additionally, some investigators reported that SampEn increased as noise increased [11]. However, for the SampEn1 of the COP's position, there was no significant change between EO and EC for almost EDSS scores and the difference among the patients was not significant. The possible explanation for these observations is that the difference of the SampEn1 may be offset by the tolerance which depends on the variation of the time series, i.e. the standard deviation.

In contrast to the results obtained for SampEn1 and SampEn2 in our study, Huisinga et al. found that patients with MS exhibit increased regularity (decreased approximate entropy, AnEn) during standing compared to healthy controls [6]. Just like SampEn, ApEn computes the likelihood that fluctuation patterns repeat themselves in a given time series [11]. The first possible reason is that EDSS scores for their patients (mean of 4.5) are higher than ours (all < 4). That means their patients have the impairment to walking. Our patients are not in the same level of MS. The second possible explanation is the duration of the experiment. Their test lasted 5 min whereas our test lasted only 51.2 s. That is why fatigue presented during their test. Fatigue inevitably affects the analysis results. The third possible reason is the sampling frequency of the used force platform. Their sampling frequency is 10 Hz while our one is 40 Hz. SampEn has been reported to be affected by the sampling frequency [11].

V. Conclusion

In this paper, we evaluated the postural sway in MS using two nonlinear parameters, TREND and SampEn. The results have shown that, compared to TREND and SampEn1, SampEn2 is able to classy the MS patients of different EDSS scores in the eyes closed. Thanks to the multi-dimensional nonlinear analysis, some hidden information in the COP data could be extracted to quantify disability in MS.

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